Comparison of the efficacy of broad-band targeted UVB phototherapy and topical psoralen with targeted UVA phototherapy in localized vitiligo

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Running title: **Targeted phototherapy in localized vitiligo**

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Abstract

Aim: To compare efficacy of targeted broad-band UVB phototherapy and topical psoralen with targeted UVA phototherapy treatments in localized vitiligo for three months prospectively.

Material and Methods: The cases with symmetrical vitiligo lesions were included in the study. Broad-band targeted UVB was applied on one side and targeted UVA phototherapy with topical psoralen on the other side.

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Results: Twenty-two patients who were diagnosed with localized vitiligo were enrolled in this study. These cases consisted of 6 (27,3%) females and 16 (72,7%) males aging between 17-69 (34,22±14,15). Fifty-four lesions (27 left, 27 right) were compared for treatments. After the first month of the treatments, the sides of the lesions were compared in order to evaluate improvement. Percentages of success were 25% for targeted broad-band UVB microphototherapy and 75% for topical psoralen with targeted UVA microphototherapy. When the two treatment methods were compared with each other, a significant difference was found in terms of treatment response. (p=0,017). At the end of the third month, the success rates were 37,5% for targeted broad-band UVB microphototherapy and 62,5% for topical psoralen with targeted UVA microphototherapy, however a statistically significant difference was not determined between the two treatments (p>0,05).

Conclusion: Both targeted broad-band UVB phototherapy and topical psoralen with targeted UVA phototherapy provided repigmentation for localized vitiligo at the end of the third month. Our investigation shows that both treatments are safe and they provide repigmentation with a limited response.

Key words: vitiligo, targeted, phototherapy

Introduction

Vitiligo is a common idiopathic, acquired depigmentation disease characterized by milky white colored, generally well-circumscribed, round, oval or linear shaped, sharply demarcated depigmented lesions ranging in size from a few millimeters to a few centimeters. The incidence of this disease varies between 1-2%. According to many researchers, the disease is most likely multifactorial and polygenic in origin. The etiopathogenesis is not fully known, which leads to the lack of a satisfactory treatment option. Current treatments are unfortunately limited in the success of vitiligo treatment.

Microphototherapy which is also named as targeted phototherapy or selective phototherapy, is a form that can deliver much higher UV doses than what can be given with classical phototherapy methods in a short time, only to the lesions to be treated and preventing unnecessary light exposure of non-lesional areas, thus reducing the risk of erythema and long-term cancer. It allows the energy to be sent quickly, thus shortening the treatment time. By sending high-dose energy to the lesion selectively, the effectiveness of the treatment increases and the response to the treatment is obtained faster (1).

In this study, it was aimed to compare the effectiveness of light-based targeted broad-band UVB microphototherapy, which is one of the most popular microphototherapy systems in vitiligo treatment, and topical psoralen with targeted UVA microphototherapy,

Materials and Methods

Twenty-two patients between the ages of 12-65 who applied to the outpatient clinic with a diagnosis of localized and symmetrically distributed vitiligo for the last 5 years who had not received topical therapy for the last 2 weeks and phototherapy for the last 4 weeks were included in our study regardless of gender.

Patients with a history of hypertrophic scar, melanoma or other skin cancers, those who had one or more of the diagnoses of photosensitivity diseases, pregnant women, breastfeeding patients, those who were allergic to topical psoralene and those receiving immunosuppressive therapy were not included in the study. For the study; a drug research local ethics committee report was obtained(1491-609-09/1539).

The treatment was planned for 36 sessions (3 months) 3 days a week. The initial treatment doses of the patients were determined as 1.0 J/cm2 in PUVA treatment, and a dose increase of 0.5 J/cm2 was made in each session. The initial doses for targeted broad-band UVB microphototherapy were determined as 40 mJ/cm2 for those with phototype III and 50 mJ/cm2 for those with phototype IV, according to the skin phototype of the patients. The doses were increased by 10 mJ/cm2 in each session. Photographs of the patients were taken before the treatment and at the end of the 1st and 3rd months after the treatment. Vitiligo Disease Activity (VIDA) scoring of each patient was made before starting the treatment. The pictures taken with the help of Corel Draw X3 version 13 computer program were squared (each square=1cm2) and the improvement in the lesions was recorded using morphometric analysis. The data obtained by counting the improved squares were calculated by statistical methods using continuous parameters. Besides, the improvement at the end of the 1st and the 3rd months was determined by the same clinician by using a 5 point scale (0-no repigmentation, 1-24% repigmentation, 2- repigmentation 25-49%, 3- repigmentation 50-74%, 4-repigmentation 75-99% 5- full repigmentation).

"SPSS for Windows version 17.0" (Statistical Program for Social Sciences) program was used for the statistical evaluation of the study results. Chi-square test was used to compare discrete parameters of independent groups, Mann Whitney U test was used to compare

continuous parameters, Mc Nemar test was used to evaluate discrete parameters of dependent groups, and Wilcoxon test was used to evaluate continuous parameters.

Results:

A total of 22 patients diagnosed with clinically localized vitiligo were included in our study. All of the patients completed the study. Six of the cases were female (27,3%), and 16 were male (72,7%). The age of the patients ranged between 17 and 69 years and the mean age was calculated as 34.22±14.15 (arithmetic mean=AO±standard deviation=SD). Fifty-four lesions (27 left, 27 right) were compared in terms of response to topical psoralen with targeted UVA microphototherapy and targeted broad-band UVB therapy, 2 regions were taken into consideration seperately in 5 patients.

The activity of vitiligo disease was evaluated by VIDA scoring. VIDA scores were recorded as -1 in 2 patients, 0 in 6 patients, +1 in 5 patients, +2 in 1 patient, +3 in 5 patients, and +4 in 3 patients **(Table 1)**.

Lesions to be treated on one half of the body were located as follows: 8 (29,6%) in the leg and/or knee area, 9 (33,3%) in the arm and/or elbow area, 4 (14,8%) in the trunk and/or waist area, 4 (14,8%) in the face area and 2 (7,4%) in the foot area.

From the lesions squared with the Corel Draw X3 program [1 square=1cm2], the number of frames was deducted according to the recovery status, and and as a result, when both treatment methods are evaluated within themselves; the initial states of the lesions and their condition at the end of the 3rd month of the treatment were significantly different in terms of response to treatment ($p < 0,05$).

While 55,6% of the lesions on the right side responded to the treatment, 44,4% did not and while 33,3% of the lesions on the left responded to treatment, 66,7% did not. When the lesions on the right side that responded to treatment were evaluated in terms of the treatment regions; 40% of the lesions in the leg-knee region, 20% of the lesions in the arm-elbow region, 20% of the lesions in the body-waist region and 20% of the lesions in the face region responded to the treatment. There was no response to the treatment in the foot region.

When the response of the lesions on the right side is compared with the response of the lesions on the left side at the end of the 1st month of the treatment; while there was a response in 12 of the 27 lesions on the right side, no response was seen in 15 and there was a response in 4 of the 27 lesions on the left side, whereas no response was seen in 23 of them. Treatment

success rate was 75% on the right and 25% on the left. The difference in response between the two treatments was significant according to the chi-square test (p=0.017).

Considering the number of the lesions with repigmentation, repigmentation was achieved between 1-24% in 11 and 25-49% in 1 of 27 lesions on the right, and 1-24% in 4 of the lesions on the left **(Figure 1).** At the end of the 1st month, topical psoralen + targeted UVA microphototherapy was found to be more successful than targeted broad-band UVB therapy in vitiligo treatment. The responses of the targeted broadband UVB and topical psoralen with targeted UVA are seen on figure **(Figure 2-3-4-5).**

When the success percentages of the treatments against each other at the end of the 3rd month were compared; while 62,5% of the patients who received topical psoralen with targeted UVA microphototherapy on the right side had a response to the treatment, this percentage was found to be 37,5% in those patients who received targeted UVB treatment on the left side. When these results were compared, no statistically significant difference was found between the groups (p>0.05).

When patients' age and the response to treatment were compared, the response to treatment with both targeted broad-band UVB therapy and topical psoralen with targeted UVA therapy was observed more in the patients who were older than 30 years old than the ones who were younger. When the patients' response to the treatments were compared with the VIDA scores, no significant relationship was found between the VIDA scores and the response to the treatments (p>0.05).

Discussion

Vitiligo is an acquired disease that is difficult and and takes time to treat; the current treatments have limited success due to the lack of clarity of the etiopathogenesis. While narrow-band UVB and psoralen with UVA constitute the first-line treatment in patients with generalized vitiligo where more than 10-20% of the body surface is involved, topical treatments such as topical corticosteroids or calcineurin inhibitors stand out as the first step of the therapy to be used in patients with localized vitiligo (2). Recently, microphototherapy and narrow-band excimer laser treatment options are among the current approaches (3).

Whole body phototherapy is not suitable in patients with localized vitiligo, as patients will get unnecessary light and cancer risks will increase in the long term. Microphototherapy which is one of the current treatment approaches, is becoming more popular day by day in localized vitiligo, as it prevents unnecessary light in non-lesional areas, thus reducing the risk

of erythema and cancer in the long term, shortening the treatment period and providing ease of treatment even in difficult areas (1).

Most of the studies on the effectiveness of microphototherapy on vitiligo lesions consist of studies which were performed about 308nm excimer laser and monochromatic excimer light therapy (4,5). Only a few studies have shown that broad-band and narrow-band targeted microphototherapy using light-based microphototherapy devices are effective in vitiligo treatment (6,7,8). Besides, studies showing that targeted UVA microphototherapy is effective in vitiligo is lacking in the literature . Only in one study conducted by Koh et al. on Asian children, thirty-nine patients were treated using the targeted phototherapy device using the combined UVA1/UVB mode; 22 had vitiligo vulgaris, 13 had segmental vitiligo, 3 had lip-tip involvement, and 2 had focal involvement with predominantly facial lesions. Twenty-six patients (67%) reported good response, eight (21%) reported poor response, and four (10%) did not complete treatment and were lost to follow-up. The mean number of treatment sessions required was 50.3 (range 5–209). Seventeen patients eventually required treatment using a different phototherapy modality. Sixty-two percent of patients experienced some side effects with the combined UVA1 and UVB targeted treatments, with 19 patients having posttreatment erythema. Blistering was seen in three patients, with pain and skin peeling being less commonly reported (9) Spencer et al. applied 308 nm xenon-chloride excimer laser to 20 localized vitilligo lesions of 18 patients three days a week, and at the end of 6 sessions, 57% repigmentation was observed.. The repigmentation score was found to be higher in the periocular region (4).

Suhail et al applied 308-nm excimer laser on 55 vitiligo lesions for 30 sessions two days a week, and they observed more than 75% of repigmentation in 50% of the patients, being more effective in the facial area (10).

Hui-Lan et al. compared the effectiveness of the usage of 308-nm excimer laser alone and in combination with pimecrolimus cream in symmetrical vitiligo lesions of 49 pediatric patients. They reported that the 308-nm excimer laser was more effective in facial and trunk lesions, and they suggested that there was no statistically significant difference between its combination with pimecrolimus cream and its use alone (11).

In his study, Xiang applied monochromatic excimer light on 201 vitiligo lesions and provided repigmentation in 92 lesions after the first 4 sessions. At the end of 6 months, different degrees of repigmentation were achieved in 174 of 201 lesions (12).

Welsh et al. applied targeted narrow-band UVB therapy for a total of 30 sessions two days a week on 20 patients with vitiligo with less than 10% of the body surface area involved, and as a result, they achieved repigmentation of 66.25% of the lesions in the facial region. and

31.5% repigmentation in the neck, trunk, and genital regions. However, there was no response in the acral regions (13).

Lotti et al conducted a control group study to investigate the effectiveness of targeted narrow-band UVB therapy in patients with segmental vitiligo. In 8 patients with segmental vitiligo, targeted narrow-band UVB treatment was applied for 6 months and they achieved more than 75% repigmentation in the patients. Especially in 3 patients, complete repigmentation was achieved. Repigmentation was obtained between 50% and 75% in 2 patients, and below 50% in only 1 patient. In the control group, less than 50% repigmentation was achieved in only 1 patient who received a placebo (7).

Menchini et al. evaluated the efficacy of targeted narrow-band UVB treatment in vitiligo for 12 months on 734 segmental and nonsegmental patients and provided repigmentation above 75% on 510 patients. Especially in 112 of these patients they achieved complete repigmentation. They obtained 50-75% repigmentation in 155 patients and less than 50% repigmentation in 69 patients (14).

Brazzelli et al. treated 60 patients with vitiligo with targeted narrow-band UVB phototherapy with a maximum duration of 2 years. They achieved complete repigmentation in 68% of the lesions in the facial region. In the first year of treatment, 57.89% complete repigmentation was achieved in the neck region and 50% in the trunk. In their study, they stated that if the age of the patient is less than 20 and the duration of the lesion is new, they can obtain more repigmentation (15).

In another study, Aswanonda et al. compared the efficacy of targeted broad-band UVB therapy and targeted narrow-band UVB therapy on vitiligo lesions in a double-blind, randomized study on a total of 20 lesions, and as a result of the comparison of targeted broad-band and targeted narrow-band UVB treatments they reported the efficacy to be similar (16).

In our study, the response of the UVA mode of the light-based microphototherapy system with psoralen, which was not evaluated before, was compared with the response of the broad-band UVB mode to treatment. At the end of the 1st month, the responses to the treatments were significant in favor of the combination of topical psoralen with targeted UVA microphototherapy, but at the end of the 3rd month, there was no significant difference between topical psoralen with targeted UVA microphototherapy and targeted broad-band UVB microphototherapy. It was observed that topical psoralen with targeted UVA therapy initiated repigmentation faster, but at the end of the 3rd month, the treatment response was similar to targeted broad-band UVB therapy. Although both treatment methods provide repigmentation, targeted broad-band UVB microphototherapy appears to be more effective in the facial region,

while topical psoralen plus targeted UVA microphototherapy have been found to be more successful in lesions in the leg-knee area. In the study of Koh et al. they suggested that targeted therapy using UVA1 and UVB had a response rate (67% with good response) comparable with that of NBUVB phototherapy and a better response rate than excimer lamp phototherapy (9). Nevertheless, more studies are needed to support these results due to the fact that the number of regions undergoing treatment is not equal and the number of patients participating in the study is not high. In the study, there was no significant relationship between VIDA scores and the responses to treatments. In contrast to other studies, it was found that the response to treatment was better in both topical psoralen with targeted UVA microphototherapy and targeted broad-band UVB microphototherapy in patients over 30 years of age rather than younger patients.

In conclusion, it is seen that both topical psoralen with targeted UVA microphototherapy combination and targeted broad-band UVB microphototherapy are effective and safe in the treatment of localized vitiligo. It is thought that topical psoralen with targeted UVA microphototherapy is effective in cases where the response to the treatment is desired in a shorter time and in the regions that are considered more resistant to treatment compared to facial region, such as the leg-knee and arm-elbow regions.

Data availability: The authors confirm that the data supporting the findings of this study available within the article and/or its supplementary materials.

REFERENCES

1. Mysore V. Targeted phototherapy. Indian J Dermatol Venereol Leprol2009;75:119-25.

2. Falabella R, Barona MI. Update on skin repigmentation therapies in vitiligo. Pigment Cell Melanoma Res 2009;22:42-65.

3. Lotti T, Gori A, Zanıerı F, Coloccı R, Moretti S. Vitilio: new and emerging treatments. Dermatologic Ther 2008;21:110-7.

4. Spencer JM, Nossa R, Ajmeri J. Treatment of vitiligo with the 308-nm excimer laser: a pilot study. J Am Acad Dermatol 2002;46:727-31.

5. Lu-yan T, Wen-wen F, Lei-hong X, Yi J, Zhi-zhong Z. Topical tacalcitol and 308-nm monochromatic excimer light: a synergistic combination for the treatment of vitiligo. Photodermatol Photoimmunol Photomed 20006;22:310-4.

6. Seçkin D, Ergun T. Dermatolojide 308 nm monokromatik excimer sistemleri. Turkderm 2008;42:77-81.

7. Lotti TM, Menchini G, Andreassi L. UV-B radiation microphototherapy. An elective treatment for segmental vitiligo. J Eur Acad Dermatol Venereol 1999;13:102-8.

8. Akar A, Tunca M, Koc E, Kurumlu Z. Broadband targeted UVB phototherapy for localized vitiligo: a retrospective study. Photodermatol Photoimmunol Photomed 2009;25:161-3.

9. Mark Jean-Aan Koh [1], Zhun-Rui Mok, Wei-Sheng Chong. Phototherapy for the treatment of vitiligo in Asian children. Pediatr Dermatol Mar-Apr 2015;32(2):192-7.

10.Suhail M, Spencer JM, Lebwohl M. The use of the 308-nm excimer laser for the treatment of vitiligo. Dermatol Surg 2004;30:983-6.

11.Hui-Lan Y, Xiao-Yan H, Jıan-Yong F, Zong_rong L. Combination of 308-nm excimer laser with topical pimecrolimus for the treatment of childhood vitiligo. Pediatr Dermatol 2009;26:354-6.

12.Xiang L. Once- weekly treatment of vitiligo with monocromatic excimer light 308 nm in Chinese patients. J Eur Acad Dermatol Venereol 2008;22:899-900.

13.Welsh O, Herz-Ruelas ME, Gómez M, Ocampo-Candiani J. Therapeutic evaluation of UVB-targeted phototherapy in vitiligo that affects less than 10% of the body surface area. Int J Dermatol 2009;48:529-34.

14. Menchini G, Tsoureli-Nikita E, Hercogova J. Narrow-band UV-B microphototherapy: a new treatment for vitiligo. J Eur Acad Dermatol Venereol 2003;17:171-7.

15.Brazzelli V, Antoninetti M, Palazzini S, Barbagallo T, Silvestri AD, Borroni. Critical evaluation of the variants inluencing the clinical response of vitiligo: study of cases treated with ultraviolet B narrow-band phototherapy. J Eur Acad Dermatol Venereol 2007;21:1369-74.

16. Aswanonda P, Kırjluakıat J, Korkıj W, Sındhupak W. Targeted broadband ultravioet B Phototherapy produces to targeted narrowband ultraviolet B Phototherapy phototherapy for vitiligo: a randomized, double-blind study. Acta Derm Venereol 2008;88:376-81.

Table 1. VIDA scoring

Vitiligo activation	**Time**	**VIDA score**
Active	6 weeks or less	+4
Active	6 weeks -3 months	+3
Active	3-6 months	+2
Active	6-12 months	+1
Stable	1 year or more	0
Stable and spontaneous repigmentation	1 year or more	-1

Figure 1. Comparison of the repigmentation percentages and the response to treatment at the end of the 1st month

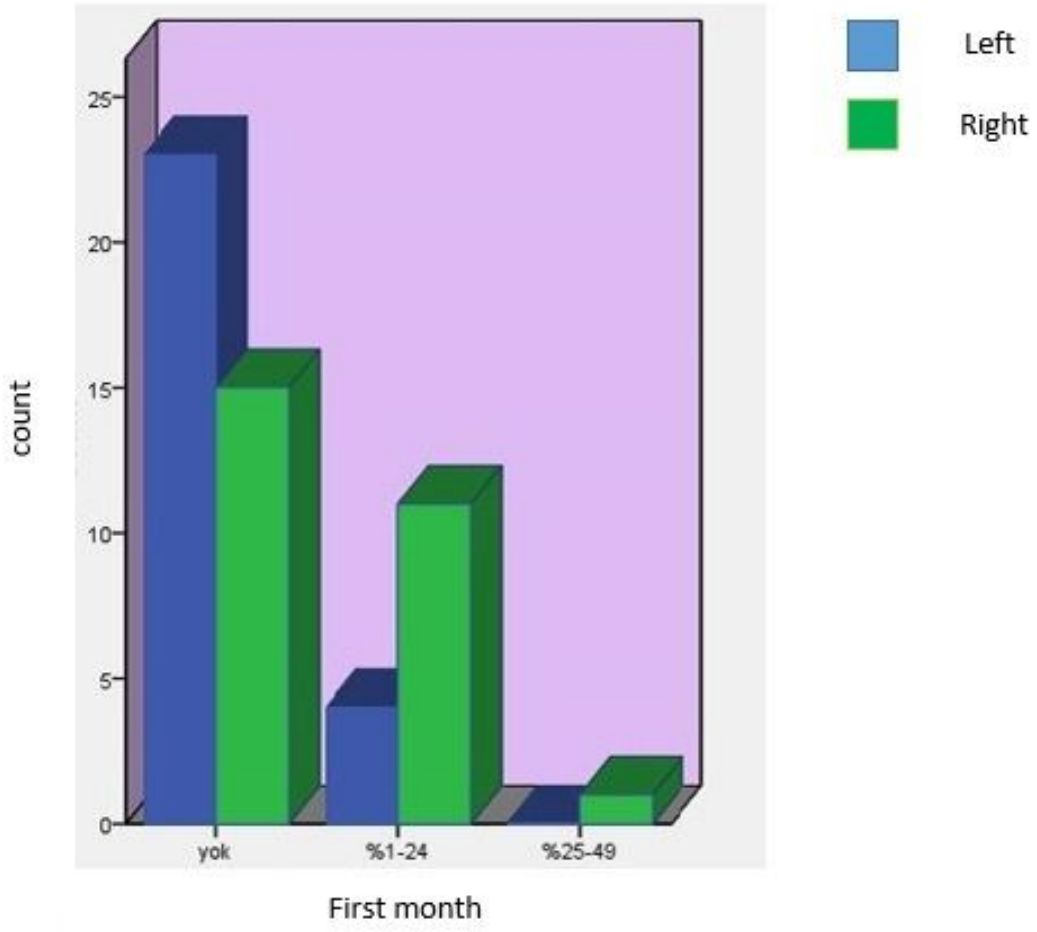

Figure 2. Topical psoralen with targeted UVA therapy: leg
before treatment [A], at the end of the 1st month [B], at the end of the 3rd month [C]

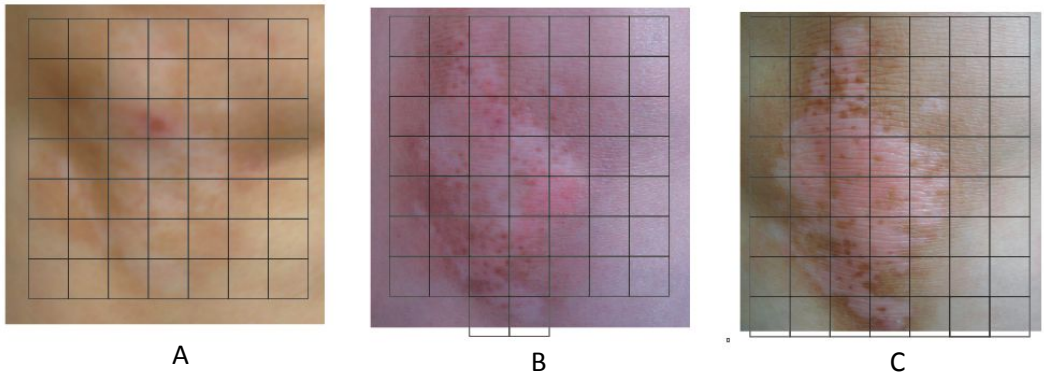

Figure 3. Targeted broad-band UVB therapy: leg
before treatment [A], at the end of the 1st month [B], at the end of the 3rd month [C]

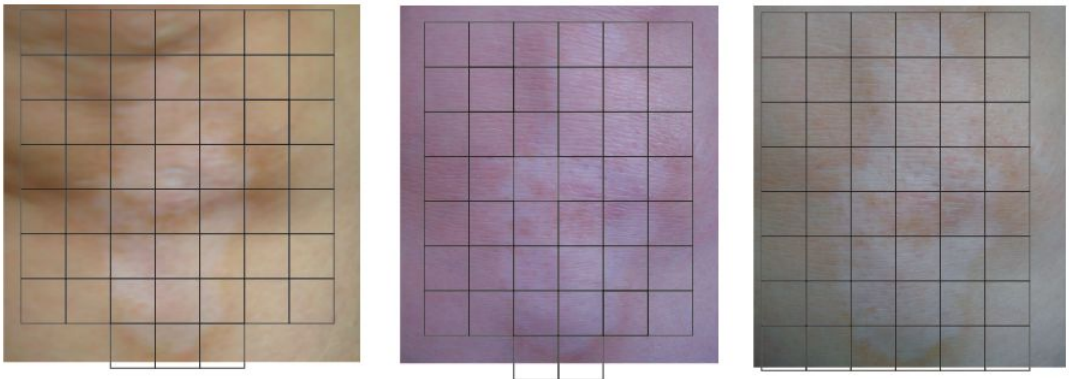

Figure 4. Topical psoralen with targeted UVA therapy: arm
before treatment [A], at the end of the 1st month [B], at the end of the 3rd month [C]

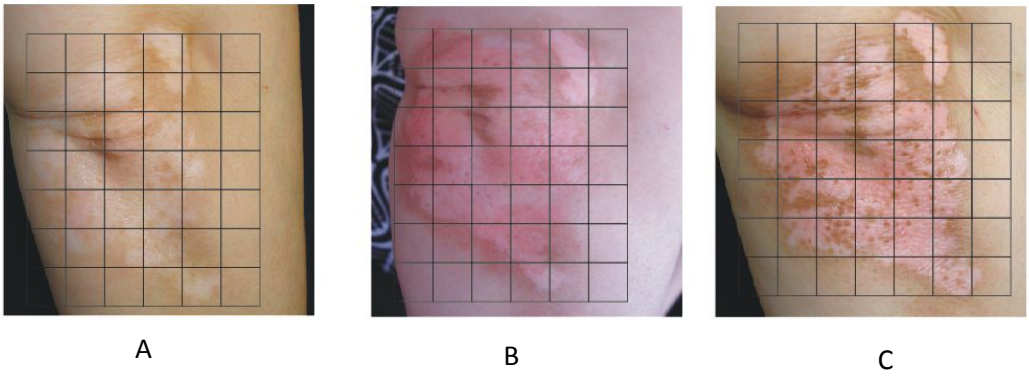

Figure 5. Targeted broad-band UVB therapy: arm

before treatment [A], at the end of the 1st month [B], at the end of the 3rd month [C]